Practitioner's Docket No. 698.26-US1

CHAPTER II

TRANSMITTAL LETTER TO THE UNITED STATES ELECTED OFFICE (EO/US)

(ENTRY INTO U.S. NATIONAL PHASE UNDER CHAPTER II)

PCT/GB00/02171	05 June 2000 (5.06.00)	04 June 1999 (4.06.99)
International Application Number	**International Filing Date**	**International Earliest Priority Date**

TITLE OF INVENTION: TISSUE REJUVENATION BY ILLUMINATING RADIATION

APPLICANT(S): ICN PHOTONICS LIMITED; KIERNAN, Michael Noel; CLEMENT, Robert Mark; and BJERRING, Peter

Box PCT
Assistant Commissioner for Patents
Washington D.C. 20231
ATTENTION: EO/US

1. Applicant herewith submits to the United States Elected Office (EO/US) the following items under 35 U.S.C. Section 371:

   a. This express request to immediately begin national examination procedures (35 U.S.C. Section 371(f)).

   b. The U.S. National Fee (35 U.S.C. Section 371(c)(1)) and other fees (37 C.F.R. Section 1.492) as indicated below:

CERTIFICATION UNDER 37 C.F.R. SECTION 1.10*
*(Express Mail label number is **mandatory.**)*
(Express Mail certification is optional.)

I hereby certify that this paper, along with any document referred to, is being deposited with the United States Postal Service on the date below, in an envelope as "Express Mail Post Office to Addressee," mailing Label Number EV 011494956 US, addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

Date: 12/4/01

Collene Houston
Collene Houston

2. Fees

CLAIMS FEE*	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
	TOTAL CLAIMS	27 -20	7	x $18.00 =	$ 126.00
	INDEPENDENT CLAIMS	4 - 3	1	x $84.00 =	$ 84.00
	MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $280.00	$ 0.00
BASIC FEE	**U.S. PTO WAS NOT INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY** Where no international preliminary examination fee as set forth in Section 1.482 has been paid to the U.S. PTO, and payment of an international search fee as set forth in Section 1.445(a)(2) to the U.S. PTO: where a search report on the international application has been prepared by the European Patent Office or the Japanese Patent Office (37 C.F.R. Section 1.492(a)(5)) $890.00				$ 210.00
	Total of above Calculations				$1,100.00
SMALL ENTITY	Reduction by 1/2 for filing by small entity, if applicable. Affidavit must be filed. (note 37 CFR Sections 1.9, 1.27, 1.28)				$ 550.00
	Subtotal				$ 550.00
	Total National Fee				$ 550.00
	Fee for recording the enclosed assignment document $40.00 (37 C.F.R. Section 1.21(h)). See attached "ASSIGNMENT COVER SHEET".				$ 0.00
TOTAL	Total Fees Enclosed				$ 550.00

*See attached Preliminary Amendment Reducing the Number of Claims.

A check in the amount of $550.00 to cover the above fees is enclosed.

3. A copy of the International application as filed (35 U.S.C. Section 371(c)(2)) was transmitted by the International Bureau on February 9, 2001.

4. A translation of the International application into the English language (35 U.S.C. Section 371(c)(2)) is not required as the application was filed in English.

5. Amendments to the claims of the International application under PCT Article 19 (35 U.S.C. Section 371(c)(3)) have not been transmitted. Applicant chose not to make amendments under PCT Article 19.

6. A translation of the amendments to the claims under PCT Article 19 (38 U.S.C. Section 371(c)(3)) has not been transmitted for reasons indicated in section 5.

7. A copy of the international examination report (PCT/IPEA/409) is transmitted herewith.

8. Annex(es) to the international preliminary examination report is/are transmitted herewith.

9. A translation of the annexes to the international preliminary examination report is not required as the annexes are in the English language.

10. An oath or declaration of the inventor (35 U.S.C. Section 371(c)(4)) complying with 35 U.S.C. Section 115 will follow.

11. An International Search Report (PCT/ISA/210) or Declaration under PCT Article 17(2)(a) was transmitted by the International Bureau on 22 September 2000.

12. An Information Disclosure Statement under 37 C.F.R. Sections 1.97 and 1.98 will be transmitted within THREE MONTHS of the date of submission of requirements under 35 U.S.C. Section 371(c).

13. Additional documents:
    a. International Publication No. WO00/74782 and Specification, claims and drawing
    b. Form PCT/IB/306 and Certificate of Incorporation on Name Change

14. The above items are being transmitted before 30 months from any claimed priority date.

AUTHORIZATION TO CHARGE ADDITIONAL FEES

The Commissioner is hereby authorized to charge the following additional fees that may be required by this paper and during the entire pendency of this application to Account No.: 500341

37 C.F.R. Section 1.492(a)(1), (2), (3), and (4) (filing fees)
37 C.F.R. Section 1.492(b), (c), and (d) (presentation of extra claims)
37 C.F.R. Section 1.17 (application processing fees)
37 C.F.R. Section 1.17(a)(1)-(5) (extension fees pursuant to Section 1.136(a))
37 C.F.R. Section 1.492(e) and (f) (surcharge fees for filing the declaration and/or filing an English translation of an International Application later than 20 months after the priority date).

Date: 4 Dec 2001

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
WASHINGTON, D.C. 20231

Inventor: **Michael Kiernan & Robert Clement**

Serial No: **US national phase of PCT/GB00/02171**

Filed: **June 5, 2000**

For: **Tissue Rejuvenation by Illuminating Radiation**

Examiner: **Not yet determined**

Art Unit: **Not yet determined**

PRELIMINARY AMENDMENT

The Honorable Commissioner
of Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

Please enter the following as a preliminary amendment.

IN THE CLAIMS

The amended claims are as follows:

4. (Amended) A process according to claim 1 wherein the illuminating radiation exits illuminating radiation apparatus externally of the body of which the tissue structure forms a part.

5. (Amended) A process according to claim 1, wherein the illuminating radiation exits illuminating radiation apparatus internally of the body or organism of which the tissue structure forms a part.

7. (Amended) A process according to claim 1, wherein the absorption of the radiation by the target structure at the predetermined low level controlled dose stimulates collagen regrowth.

8. (Amended) A process according to claim 1, wherein the illuminating radiation dose is controlled to ensure that overdosing of the target tissue structure does not take place.

9. (Amended) A process according to claim 1, wherein the wavelength of the illuminating radiation is selected such that there is at least some absorption by the target structure or tissue.

10. (Amended) A process according to claim 1, wherein the radiation delivered is light, substantially in the wavelength bandwidth 400-1500nm.

11. (Amended) A process according to claim 1, wherein the radiation delivered is light, substantially in the wavelength bandwidth 500-1000nm.

12. (Amended) A process according to claim 1, wherein the illuminating radiation is of a discrete wavelength or relatively narrow wavelength bandwidth.

13. (Amended) A process according to claim 1, wherein the illuminating radiation is of a relatively broad band light source filtered to a discrete or relatively narrow wavelength bandwidth.

14. (Amended) A process according to claim 1, wherein the illuminating radiation is laser radiation.

15. (Amended) A process according to claim 1, wherein the illuminating radiation is obtained from an LED.

16. (Amended) A process according to claim 1, wherein the illuminating radiation is obtained from a broad band white light source.

17. (Amended) A process according to claim 1, wherein a body tissue structure is illuminated by means of direct external illumination of the structure.

18. (Amended) A process according to claim 1, wherein the illuminating radiation is directed into the body to be delivered to the site of an internal target tissue structure.

19. (Amended) A process according to claim 1, wherein the energy density of the illuminating radiation delivered to the target structure is substantially in the range 2 to 20Jcm-2.

20. (Amended) A process according to claim 1 for inducing a controlled inflammatory response in one or more of the following collagen containing structures:

bone
dentin
cartilage
uterus
large veins and arteries.

23. (Amended) Apparatus according to claim 21, wherein the means for directing the radiation to the target site is configured to permit manual manipulation enabling the zone of radiation impingement with the target site to be manually altered.

24. (Amended) Apparatus according to claim 21, wherein the apparatus is provided with an automated drive arrangement.

25. (Amended) Apparatus according to claim 21, including pulsation means for pulsing the illuminating radiation, preferably having a pulse duration substantially in the range 1 microsecond- 100ms.

26. (Amended) Apparatus according to claim 21, including scanning means for scanning the illuminating radiation over the target tissue structure.

REMARKS

The requested changes merely remove multiple dependencies.

Respectfully submitted,
Fish & Associates, LLP

Dated: 4 Dec 2001

By: _____
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VERSIONS WITH MARKING TO SHOW CHANGES MADE

In the Claims

4. (Amended) A process according to ~~any preceding~~ claim 1 wherein the illuminating radiation exits illuminating radiation apparatus externally of the body of which the tissue structure forms a part.

5. (Amended) A process according to ~~any of~~ claims ~~1 to 3~~, wherein the illuminating radiation exits illuminating radiation apparatus internally of the body or organism of which the tissue structure forms a part.

7. (Amended) A process according to ~~any preceding~~ claim 1, wherein the absorption of the radiation by the target structure at the predetermined low level controlled dose stimulates collagen regrowth.

8. (Amended) A process according to ~~any preceding~~ claim 1, wherein the illuminating radiation dose is controlled to ensure that overdosing of the target tissue structure does not take place.

9. (Amended) A process according to ~~any preceding~~ claim 1, wherein the wavelength of the illuminating radiation is selected such that there is at least some absorption by the target structure or tissue.

10. (Amended) A process according to ~~any preceding~~ claim 1, wherein the radiation delivered is light, substantially in the wavelength bandwidth 400-1500nm.

11. (Amended) A process according to ~~any preceding~~ claim 1, wherein the radiation delivered is light, substantially in the wavelength bandwidth 500-1000nm.

12. (Amended) A process according to ~~any preceding~~ claim 1, wherein the illuminating radiation is of a discrete wavelength or relatively narrow wavelength bandwidth.

13. (Amended) A process according to ~~any preceding~~ claim 1, wherein the illuminating radiation is of a relatively broad band light source filtered to a discrete or relatively narrow wavelength bandwidth.

14. (Amended) A process according to ~~any preceding~~ claim 1, wherein the illuminating radiation is laser radiation.

15. (Amended) A process according to ~~any preceding~~ claim 1, wherein the illuminating radiation is obtained from an LED.

16. (Amended) A process according to ~~any preceding~~ claim 1, wherein the illuminating radiation is obtained from a broad band white light source.

17. (Amended) A process according to ~~any preceding~~ claim 1, wherein a body tissue structure is illuminated by means of direct external illumination of the structure.

18. (Amended) A process according to ~~any of~~ claims ~~1 to 11~~, wherein the illuminating radiation is directed into the body to be delivered to the site of an internal target tissue structure.

19. (Amended) A process according to ~~any preceding~~ claim 1, wherein the energy density of the illuminating radiation delivered to the target structure is substantially in the range 2 to 20Jcm-2.

20. (Amended) A process according to ~~any preceding~~ claim 1 for inducing a controlled inflammatory response in one or more of the following collagen containing structures:

bone
dentin
cartilage
uterus
large veins and arteries.

23. (Amended) Apparatus according to claim 21 ~~or claim 22~~, wherein the means for directing the radiation to the target site is configured to permit manual manipulation enabling the zone of radiation impingement with the target site to be manually altered.

25. (Amended) Apparatus according to ~~any of~~ claims 21 ~~to 23~~, wherein the apparatus is provided with an automated drive arrangement.

25. (Amended) Apparatus according to ~~any of~~ claims 21 ~~to 23~~, including pulsation means for pulsing the illuminating radiation, preferably having a pulse duration substantially in the range 1 microsecond- 100ms.

26. (Amended) Apparatus according to ~~any of~~ claims 21 ~~to 25~~, including scanning means for scanning the illuminating radiation over the target tissue structure.

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TISSUE REJUVENATION BY ILLUMINATING RADIATION

The present invention relates to tissue rejuvenation and in particular to tissue rejuvenation by means of selective production of collagen at a target site.

The human body has a variety of different types of collagen, which essentially constitute the extracellular matrix of the body. This matrix is the material that binds and supports cells and is essential for the survival of a multicellular organism. Collagens provide the tissue with tensile strength.

The various collagen containing structures in the body include bone, dentin, cartilage, uterus and the larger vessels in the circulatory system. As the body ages the rate of collagen naturally decreases leading to breakdown in tissue and organ structure and function. Other problems can also exacerbate or cause tissue or organ structure deterioration due to inhibition of collagen formation.

According to a first aspect, the invention comprises a technique for stimulating collagen containing structures, the technique comprising illuminating a target structure with illuminating radiation causing elevation of the temperature of a target structure, the radiation dosed to the target being controlled to induce a predetermined and precise inflammatory response in the target tissue.

The absorption of the radiation by the target structure at the predetermined low level controlled dose (resulting in the inflammatory response of the target structure tissue) stimulates collagen regrowth.

It is important that the radiation dose is controlled to ensure that overheating of the target tissue structure does not take place. Overdosing of energy (radiation) leads to thermal damage inhibiting the inflammatory phase resulting in less than optimum collagen formation. It is important therefore that the radiation energy dose delivered is of sufficiently low intensity and power to avoid tissue destruction. The radiation dose is therefore controlled dependent upon the body structure or tissue being illuminated but in all cases the intensity and duration of the illuminating radiation is relatively low level to prevent damage of the target structure or tissue.

The wavelength of the illuminating radiation is selected such that there is at least some absorption by the target structure or tissue.

In a preferred embodiment the radiation delivered is electromagnetic energy, preferably light, desirably substantially in the bandwidth 400-1500nm (more preferably substantially in the bandwidth 500-1000nm).

The illuminating radiation may be generated by laser, laser diode, light emitting diode, or a broad band white light source. The illuminating radiation is preferably of

a discrete wavelength or relatively narrow wavelength bandwidth. For a broad band white light source an appropriate filter is preferably provided.

Where the illuminating radiation is laser radiation, the laser may, for example comprises pulsed dye laser (585nm), an Argon Iron laser (514nm), Ti:Saphire laser (400nm-1100nm), Ruby laser(694nm), Nd:YAG laser (1064nm), or Frequency Doubled Nd:YAG laser (532nm).

a suitable laser diode would be a Gallium Arsenide laser diode at 630-690nm or 790-980nm.

LED's at wavelengths substantially in the range 550-1000nm would be suitable.

The technique can be used on a variety of body tissue structures either by means of direct external illumination of structures or by means of directing the illuminating radiation into the body (for example along a suitable waveguide) to be delivered to the site of the internal target structure.

According to a second aspect, there is provided apparatus for use in effecting refurbishment of tissue and/or tissue structures, which apparatus includes:

i) a source of illuminating radiation; and,

ii) means for directing the illuminating radiation

to a target site.

The means for directing the illuminating radiation to the target site preferably includes focussing means (for example optical focussing means). The means for directing the illuminating radiation to the target site preferably includes a flexible optical line including a distal portion through which the radiation is emitted in order to illuminate the target structure. The optical line may comprise an optical waveguide such as a length of fibreoptic.

The means for directing the illuminating radiation to the target site is preferably configured to permit manual manipulation enabling the zone of radiation impingement with the target site to be manually altered. Alternatively, the apparatus may be provided with an automated drive arrangement.

Desirably, the illuminating radiation is pulsed, preferably having a pulse duration substantially in the range 1 microsecond-100ms. Alternatively, scanning of illuminating radiation can produce a similar effect, in that localised tissue is irradiated only for the required short time period to deliver the appropriate energy dose.

The invention will now be further described in specific embodiments by way of example only, and with reference to the accompanying drawings, in which:

Figure 1 is a schematic representation of a first embodiment of a technique according to the invention,

Figure 2 is a schematic representation of a second embodiment of a technique according to the invention;

Figure 3 is a schematic representation of a further embodiment of a technique according to the invention;

Figure 4 is a schematic representation of a further embodiment of a technique according to the invention;

Figure 5 is a schematic representation of a further embodiment of a technique according to the invention; and,

Figure 6 is a schematic representation of a further embodiment of a technique according to the invention.

Referring to the drawings, and initially to Figure 1, there is shown a tissue rejuvenation technique in which an arrangement 1 includes a light source 2, such as an LED, laser diode or other laser or a white light source (provided with an appropriate filter), having a wavelength in a narrow bandwidth in the range 550-1000nm, directs a beam 3 via focussing optics 4 into a fibreoptic waveguide 5. Light emitted from the distal end of fibreoptic waveguide 5 passes through a collimating lens 6 where it is directed to illuminate the surface of a tissue structure 7.

In the embodiment shown in Figure 2, the beam 3 emitted from light source 2 passes directly through a focussing lens 16 which focusses the beam onto the tissue structure 7.

In the embodiment shown in Figure 3, the beam 3 from the light source 2 is directed to a scanning optical arrangement comprising rotating scanning mirrors 9, 10 arranged to scan the beam in orthogonal X-Y directions onto the tissue 7.

In each of the embodiments shown in Figures 1 to 3, the relevant tissue structure 7 is directly illuminated from externally of the body (extra-corporeal illumination).

The intensity and duration of the light beam illuminating the tissue 7 is controlled such that the energy dosed to the tissue is at a level where collagen formation is promoted, without the tissue being "injured" to a degree at which structural integrity of the tissue deteriorates. Illumination promoting collagen production mirroring wound healing in the inflammatory, proliferate and remodelling phases results in collagen production and enhancement of the structural integrity of the tissue.

It is important that the wavelength of the light illuminating the tissue is selected to have at least a component which is selectively absorbed to the required degree by the tissue in question. Appropriate selection of the wavelength to be absorbed by the tissue, or a

chromophore at or below the tissue surface, can enable discrete target sites at or below the tissue surface to be targeted.

The arrangements shown in Figure 4 to 6 relate to interstitial rejuvenation techniques where an extra corporeal light source 2 produces a beam 3 which can be directed through the body surface interface to target an internal cell structure 11, 12.

In the embodiment shown in Figure 4, the light beam 3 is focussed into a fibreoptic waveguide 5 which extends through a sheathing catheter 13. Light emanating from the end of fibreoptic waveguide 5 illuminates the target structure 11 below the body surface 14.

In the embodiments shown in Figures 5 and 6, the fibreoptic waveguide 5 extends into and along a target vessel 12 which comprises the circulatory system of the body (such as for example an artery).

In the embodiment of Figure 5, light is reflected from a mirror end 15 to illuminate the desired "target" portion of the internal vessel wall 12.

In the embodiment shown in Figure 6, the fibreoptic waveguide 5 is provided with a diffusing end 16 arranged to diffuse the light to illuminate radially the entire "target" portion of the vessel wall 12.

Illumination of the relevant tissue target structure with illuminating radiation of the required wavelength and dosage produces the inflammatory/wound healing response promoting the maximum degree of collagen formation. Promotion of collagen at the target site effectively rejuvenates the target tissue/structure.

To test the efficacy of the invention, examples have been performed using laser radiation and measuring terminals of Type III collagen produced.

When Type III collagen is formed, the molecule is in the form of a long chain with two terminals on either end. When three collagen molecules have been produced, the molecules bond together and the terminals on either end of the chain separate and are released into the dermal interstitial fluid. By measuring the quantity of the terminals in the fluid, the rate of collagen production can be measured.

As an example of the technique, biochemical investigations have shown that the production rate of Type III collagen in the dermal region of the skin can be increased by the application of the following laser parameters:

Wavelength:	585nm
Pulse Duration:	350μsec
Energy Density:	2.4J/cm^2
Spot Size:	5mm Diameter

delivered to the surface of the skin via a flexible fibre optic.

When the skin was irradiated with these parameters, the production rate of Type III collagen in the skin increased by 84%.

Similar tests performed with a Frequency Doubled Nd:YAG laser operating at the following parameters:

Wavelength:	532nm
Pulse Duration:	2msec to 20msec
Energy Density:	2-20J/cm^2
Spot Size:	3mm (dia)

showed an increase of between 22% and 44% in the Type III Collagen production rate.

Both tests were performed by treating a selected area of skin with the prescribed laser parameters and waiting 72 hours before raising suction blisters on the treated and untreated control areas. The interstitial fluid collected from the suction blisters was analysed using an immunoflourescent technique to measure the quantity of the amino-propeptide terminal of the Type III collagen molecule (PIIINP).

The quantity of PIIINP found in the blister fluid is related to the amount of Type III collagen being produced at the investigation site. The percentage increase

figures quoted are relative to adjacent control sites.

Claims:

1. A process for stimulating collagen containing structures, the process comprising illuminating a target structure with illuminating radiation causing elevation of the temperature of the target structure, the radiation dosed to the target being controlled to induce an inflammatory response in the target tissue.

2. A process according to claim 1, wherein the target tissue structure is illuminated directly, without the illuminating radiation passing significantly through extraneous tissue.

3. A process according to claim 2, wherein tissue extraneous to the target tissue structure is bypassed.

4. A process according to any preceding claim wherein the illuminating radiation exits illuminating radiation apparatus externally of the body of which the tissue structure forms a part.

5. A process according to any of claims 1 to 3, wherein the illuminating radiation exits illuminating radiation apparatus internally of the body or organism of which the tissue structure forms a part.

6. A process according to claim 5, wherein the illuminating radiation exits illuminating radiation

apparatus internally of the target tissue structure.

7. A process according to any preceding claim, wherein the absorption of the radiation by the target structure at the predetermined low level controlled dose stimulates collagen regrowth.

8. A process according to any preceding claim, wherein the illuminating radiation dose is controlled to ensure that overdosing of the target tissue structure does not take place.

9. A process according to any preceding claim, wherein the wavelength of the illuminating radiation is selected such that there is at least some absorption by the target structure or tissue.

10. A process according to any preceding claim, wherein the radiation delivered is light, substantially in the wavelength bandwidth 400-1500nm.

11. A process according to any preceding claim, wherein the radiation delivered is light, substantially in the wavelength bandwidth 500-1000nm.

12. A process according to any preceding claim, wherein the illuminating radiation is of a discrete wavelength or relatively narrow wavelength bandwidth.

13. A process according to any preceding claim, wherein the illuminating radiation is of a relatively broad band light source filtered to a discrete or relatively narrow wavelength bandwidth.

14. A process according to any preceding claim, wherein the illuminating radiation is laser radiation.

15. A process according to any preceding claim, wherein the illuminating radiation is obtained from an LED.

16. A process according to any preceding claim, wherein the illuminating radiation is obtained from a broad band white light source.

17. A process according to any preceding claim, wherein a body tissue structure is illuminated by means of direct external illumination of the structure.

18. A process according to any of claims 1 to 11, wherein the illuminating radiation is directed into the body to be delivered to the site of an internal target tissue structure.

19. A process according to any preceding claim, wherein the energy density of the illuminating radiation delivered to the target structure is substantially in the range 2 to 20Jcm^{-2}.

20. A process according to any preceding claim for

inducing a controlled inflammatory response in one or more of the following collagen containing structures:

bone
dentin
cartilage
uterus
large veins and arteries.

21. Apparatus for use in stimulating collagen containing structures, which apparatus includes:

i) a source of illuminating radiation; and,

ii) means for directing the illuminating radiation to a target site.

22. Apparatus according to claim 21, wherein the means for directing the illuminating radiation to the target site includes:

(a) focussing means; and/or,

(b) an optical delivery line; and,

(c) an emitter portion (comprising the optical delivery line or associated therewith) through which the radiation is emitted in order to illuminate the target structure.

23. Apparatus according to claim 21 or claim 22, wherein the means for directing the illuminating radiation to the target site is configured to permit manual manipulation enabling the zone of radiation impingement with the target site to be manually altered.

24. Apparatus according to any of claims 21 to 23, wherein the apparatus is provided with an automated drive arrangement.

25. Apparatus according to any of claims 21 to 23, including pulsation means for pulsing the illuminating radiation, preferably having a pulse duration substantially in the range 1 microsecond-100ms.

26. Apparatus according to any of claims 21 to 25, including scanning means for scanning the illuminating radiation over the target tissue structure.

27. A beam of illuminating radiation having:

i) wavelength substantially within the range 400nm to 1100nm and being of a discrete or relatively narrow bandwidth;

ii) an energy density within the beam of 2 to 20Jcm^{-2};

for use in directly illuminating a target tissue structure wherein tissue extraneous to the target tissue structure is bypassed, the beam producing an illuminating spot size at the tissue substantially in the range 1 to 10mm diameter.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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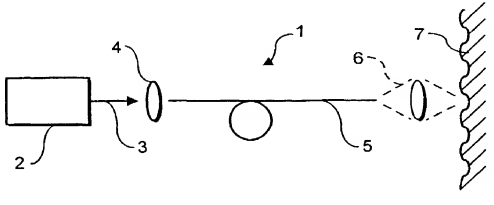
Published:
— *With international search report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette

(54) Title: TISSUE REJUVENATION BY ILLUMINATING RADIATION



(57) Abstract: Collagen containing structures are stimulated by illuminating the target structure with illuminating radiation causing elevation of the temperature of the target structure. The radiation is specifically dosed to the target being controlled to induce a precise and predetermined inflammatory response in the target tissue. The target tissue structure is illuminated directly, without the illuminating radiation passing significantly through extraneous tissue.

WO 00/74782 A1

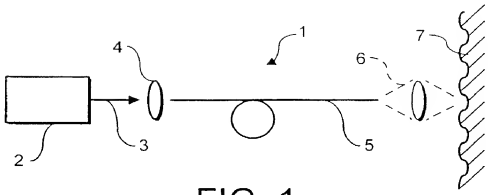


FIG. 1

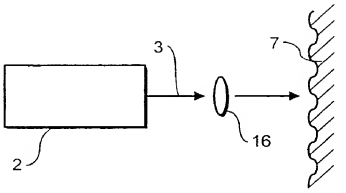


FIG. 2

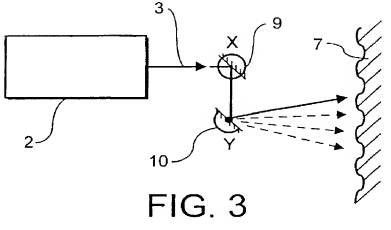


FIG. 3

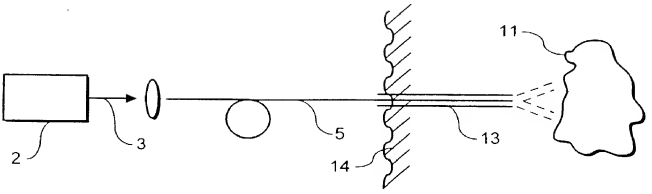


FIG. 4

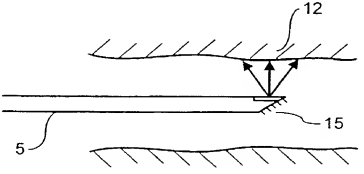


FIG. 5

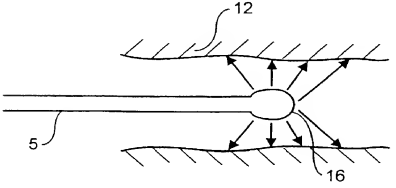


FIG. 6

Practitioner's Docket No. **698.26-US1** PATENT

COMBINED DECLARATION AND POWER OF ATTORNEY

(ORIGINAL, DESIGN, NATIONAL STAGE OF PCT, SUPPLEMENTAL, DIVISIONAL, CONTINUATION, OR C-I-P)

As a below named inventor, I hereby declare that:

TYPE OF DECLARATION

This declaration is for a national stage of PCT application.

INVENTORSHIP IDENTIFICATION

My residence, post office address and citizenship are as stated below, next to my name. I believe that I am an original, first and joint inventor of the subject matter that is claimed, and for which a patent is sought on the invention entitled:

TITLE OF INVENTION

Tissue Rejuvenation by Illuminating Radiation

SPECIFICATION IDENTIFICATION

The specification was described and claimed in PCT International Application No. PCT/GB00/02171 filed on June 5, 2000.

ACKNOWLEDGMENT OF REVIEW OF PAPERS AND DUTY OF CANDOR

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information, which is material to patentability as defined in 37, Code of Federal Regulations, Section 1.56.

PRIORITY CLAIM (35 U.S.C. Section 119(a)-(d))

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at

least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

Such applications have been filed as follows.

PRIOR PCT APPLICATION(S) FILED WITHIN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS APPLICATION AND PRIOR FOREIGN APPLICATION(S) FILED WITHIN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS APPLICATION, ANY PRIORITY CLAIMS UNDER 35 U.S.C. SECTION 119(a)-(d), AND ALL FOREIGN APPLICATION(S), *IF ANY*, FILED MORE THAN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION

INDICATE IF PCT	APPLICATION NUMBER	DATE OF FILING DAY, MONTH, YEAR
PCT	PCT/GB00/02171	5 June 2000
COUNTRY	APPLICATION NUMBER	DATE OF FILING DAY, MONTH, YEAR
United Kingdom	GB 9912877.9	4 June 1999

POWER OF ATTORNEY

I hereby appoint the following practitioner(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

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David J. Zoetewey	45,258
Sandra Poteat Thompson	46,264
Martin Fessenmaier	46,697

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SEND CORRESPONDENCE TO	DIRECT TELEPHONE CALLS TO:
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Practitioner's Docket No. **698.26-US1** PATENT

DECLARATION

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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